Danish Pharmacovigilance Update

Volume, 1 # 2
17 December 2009

Updated recommendations for antipsychotics, finasteride, statins and short-acting beta2 agonists

The following recommendations are a result of an overall review by the European Pharmacovigilance Working Party, involving an evaluation of adverse reaction data from various sources, such as adverse reaction reports, clinical studies and published literature. The recommendations wil soon be implemented in relevant summaries of product characteristics and package leaflets.

Antipsychotics and risk of venous thromboembolism

Doctors should identify possible risk factors for venous thromboembolism (VTE) in patients treated with antipsychotics, so that precautionary measures can be taken before and during treatment.

Finasteride and possible risk of male breast cancer

Doctors should advise patients who receive finasteride to report it to their doctor if they experience any changes in their breast tissue such as lumps, pain, gynaecomastia or nipple discharge.

1 mg finasteride is authorised for the treatment of hair loss in men, while 5 mg finasteride is authorised for the treatment of prostatic hypertrophy. Most of the adverse reaction reports relate to 5 mg finasteride, but a few have also been submitted for the 1 mg formulation.

Statins and possible side effects

Doctors should discontinue treatment with statins for patients who develop interstitial lung disease.

Doctors should also be aware of possible side effects such as sleep disturbance, memory loss, sexual disturbances, depression and interstitial pneumopathy.

These new findings have been added to the summary of product characteristics and package leaflet of statins, but they do not alter the overall positive risk-benefit balance of statins.

Short-acting beta2 agonists and risk of myocardial ischaemia

The use of short-acting beta2 agonists to inhibit uterine contractions is contraindicated in women with pre-existing or with significant risk factors for ischaemic heart disease

Doctors should pay special attention to asthma/COPD patients with a severe heart disease if they are treated with short-acting beta2 agonists. If heart symptoms get worse, patients must see their doctor.

Read all the recommendations at:
http://www.hma.eu/222.html

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Pandemrix® update

Period	Number of reports (number of adverse reactions)
5 - 11 Dec. 2009	68 (173)
28 Nov. - 4 Dec. 2009	77 (224)
21 - 27 Nov. 2009	149 (475)
17 - 20 Nov. 2009	87 (310)
11 - 16 Nov. 2009	73 (280)
4 - 10 Nov. 2009	13 (34
Total	**467 (1496)**

The number of adverse reaction reports submitted since 4 November totals 467, covering altogether 1496 adverse reactions.

The Danish State Serum Institute has dispensed approx. 1,000,000 vaccine doses. It is estimated that at least 370,000 people have been vaccinated in Denmark, which includes 75,000 who have been given the second dose.

Since 4 November, 82 % of adverse reaction reports have been submitted by doctors and other healthcare professionals, while 18 % have been submitted by vaccinated persons.

Read the Pandemrix® update at: *Side effects from Pandemrix® from 5 to 11 December 2009*

Young children may have fever after the second dose

Doctors should advise parents of children in an at-risk group that they may develop fever (possibly high fever) after the second dose. New data from the manufacturer show that young children from six months to three years experience more adverse reactions from the second dose than from the first dose - in particular fever, soreness at the injection site, drowsiness, irritability and loss of appetite.

If parents consider it necessary, they can give their child paracetamol, etc. to reduce fever.

Two doses, at three weeks' interval, are still recommended for children in an at-risk group younger than three years of age because the second dose provides even better protection against influenza A (H1N1).

Read the full announcement at: *Young children develop good protection from influenza A vaccine - but may have fever*

State whether it is the 1st or 2nd dose when you report side effects of Pandemrix®

The Danish Medicines Agency advise doctors to indicate whether the suspected adverse reactions relate to the first or second dose. This may help us assess whether the two vaccine doses have different safety profiles.

You can report all suspected adverse reactions at: *www.dkma.dk > Pharmacovigilance > Report a side effect*

Give one vaccine dose to:

- Patients aged 10 and older who belong to an at-risk group but have a functional immune system.
- Pregnant women who want to be vaccinated, as pregnancy in itself does not lead to a reduced effect of the vaccination.

Give two vaccine doses to:

- Children under the age of 10 in an at-risk group.
- Patients with a weakened immune system.

Read the Danish National Board of Health's recommendation at: *The National Board of Health adjusts recommendations on vaccination for influenza A (H1N1)*

List of frequently asked questions about influenza A (H1N1)v

The Danish Medicines Agency and the National Board of Health update the list of questions/answers about influenza A (H1N1)v weekly.

You can read all questions and answers at: *Questions and answers about vaccination against influenza A (H1N1)*

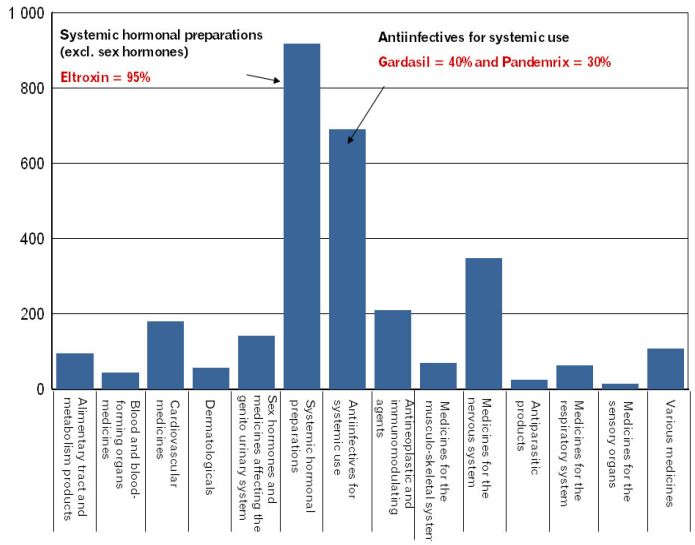
Doctors have contributed with solid data for the monitoring of Pandemrix®

From 4 November to 11 December 2009, health professionals accounted for 82 % of all adverse reactions reports related to Pandemrix®. These data have made it possible for us to assess whether the nature and frequency of the side effects experienced by the patients correspond to expectations.

Side effects from Pandemrix® from 5 to 11 December 2009

Side effects in figures

Reports by medicinal product group
(1 January - 22 November 2009)



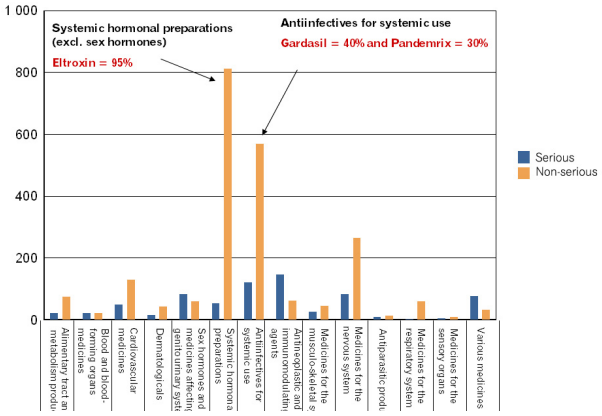
Reports by medicinal product group

The graph to the left shows the number of reports from 1 January to 22 November 2009 by therapeutic subgroups. Considering the media coverage and the medicines' extent of use, the volume of reports for the different groups corresponds to expectations.

The group of systemic hormonal preparations have received the most adverse reaction reports. In this group, Eltroxin® accounted for 95 % of the reports, which is probably a result of the widespread media coverage Eltroxin® received when GlaxoSmithKline changed the excipients and thus the formulation. The side effects emerged when patients switched from the old to the new formulation.

The group of antiinfectives for systemic use received the second-most reports. Pandemrix® and the HPV vaccine Gardasil® account for 30 % and 40 %, respectively. Both groups have received extensive media attention. All vaccines of the Danish child vaccination programme belong to this group.

Medicinal product groups and severity
(1 January - 22 November 2009)



Medicinal product groups and severity

The graph to the left shows the distribution of serious and non-serious adverse reaction reports by medicinal product groups. Most of them are non-serious, which is particularly seen for the groups containing Eltroxin® and Gardasil® and Pandemrix®.

The groups with the most serious adverse reaction reports are biological medicine and medicines for infections, which comprise vaccines. The group of various medicines contain, among other things, contrast agents such as Omniscan for which reports of nephrogenic systemic fibrosis (NSF) have been submitted.

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Four criteria make up a complete side effect report

When you report a suspected adverse reaction to the Danish Medicines Agency, the following four essential pieces of information need to be included as a minimum:

- The side effect
- The medicine
- The patient
- Reporter details.

The side effect

Diagnose the adverse reaction as precisely as possible. If the patient has experienced several side effects from the same medicine, describe them all.

The medicine

In order for us to check and monitor the safety of medicines, we need to receive as detailed information as possible about the medicine you suspect to have caused the adverse reaction. Much of the information that you must provide about the medicine is found on the package or in the package leaflet. Make every effort to name the medicine actually taken by the patient.

Beware that the medicine is not necessarily the one prescribed due to the rules on generic prescription. If in doubt, please provide information about the prescribed medicine, which you can see at the Medicine Profile via *www.sundhed.dk.*

The patient

We prefer to receive the patient's civil registration number, but otherwise the patient's sex, date of birth/age and initials will suffice. You must give at least one of these details in your report.

Reporter details

It is important that we receive details about you when you file a report so that we can contact you if we need further information. Give your full name and provider ID that refers to the practice or deparment that you are linked to.

If you enter your provider ID, the form will fill out the address fields automatically. Finally, you must provide your authorisation ID, which enables unambiguous identification.

You can report side effects at: *www.dkma.dk > Pharmacovigilance > Report a side effect*

Next year it will be easier to report side effects

In April 2010, adverse reaction reporting will be integrated in most medical practice systems across Denmark. This means that doctors will no longer need to key in the many details via the adverse reaction reporting forms used today.

Doctors will **only** need to enter a description of the side effect and the medicine thought to have caused the reaction. Details about the patient and medicine will be added directly from the Medicine Profile as will the details about the doctor based on the authorisation ID.

The following medical practice systems are comprised by the agreement between the Danish Medicines Agency and MedCom (a co-operative venture between authorities, organisations and private firms linked to the Danish healthcare sector) on the integration of reporting via the healthcare system: MyClinic, Profdoc Darwin, Ganglion, Docbase, Emar Win, MultiMed Web, MedWin, Win PLC, PC-Praxis Web, Profdoc Æskulap XMO.

You can read more about integration of adverse reaction reporting in the medical practice systems at (in Danish only): *http://www.medcom.dk/wm110660*

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Medicines with stricter reporting requirements

Remember to report all suspected adverse reactions observed within the first two years following placement on the market.Click the list below to see what medicines are subject to stricter reporting requirements.

List of medicines with stricter requirements for doctors, dentists and veterinarians to report side effects (Excel file, only in Danish)

The Danish website *www.medicin.dk* also tells you if a medicine is subject to stricter reporting requirements by listing it under the description of adverse reactions